REMARKS AND ARGUMENTS

1. The Examiner has restricted the application into the following inventions and requires restriction to one of the inventions:

I. Claims 1-4, and 6-7, drawn to a bioactive peptide to prevent or treat bacterial infections.

II. Claim 5, drawn to a peptide inhibitor against pathogenic *Escherichia coli.*

III. Claim 8, drawn to an antimicrobial peptide inhibiting polymerization of Dr. haemagglutinin.

IV. Claims 9-14, drawn to a method to treat bacterial infection by administering to the patient a therapeutically amount of bioactive peptide

V. Claims 15-16, drawn to an inhibitor molecule.

The applicant respectfully elects Group I with traverse. The applicant believes that the claims as amended above render the restriction requirement improper. The traverse is based on the following comments:

2. The Examiner argues that Group I and II are distinct, because the claims drawn to a bioactive peptide do not overlap the scope of the claims drawn to a peptide inhibitor as evidenced by the different sequences and functions of the claimed inventions. The bioactive peptide is based on sequence XTXTYY, while the peptide inhibitor is based on sequence TXTYZ. Furthermore, the Examiner states that the bioactive peptide can be used in materially different process of producing antibodies against such proteins, while the peptide inhibitor may be used in the screening of inhibitors against pathogenic *Escherichia coli* strains.

In the claims as originally submitted the applicant has used term 'bioactive peptide' in the claims now restricted to Group I, while the applicant used term 'peptide inhibitor' in

claim 5 (the only claim in Group II). The applicant has amended claims 1, 2, 3, 5, 6, and 7 so as to refer to 'antimicrobial peptide' instead of 'bioactive peptide' or 'peptide inhibitor'. The term 'antimicrobial peptide' is according to the terminology used in the specification. Moreover, the applicant has amended claim 5, so as to make it dependent of claim 2 via the newly amended claim 17.

The applicant respectfully point out that the comment of the Examiner that the bioactive peptide can be used in process of producing antibodies, while peptide inhibitors may be used in screening of inhibitors against pathogenic *E. coli* strains, is factually not correct for the following reason:

- peptides as short as those described in this application (be they called bioactive peptides, antimicrobial peptides or peptide inhibitors) can specifically NOT be used to produce antibodies due to their shortness. This is one major benefit of the current invention, because if these peptides would produce antibodies, then one would not be able to use them according to the current invention: as is shown in Figure 9, the function of the disclosed peptides according to this invention is based on the fact that the peptide is bound to the subunit of the virulence factor, thereby preventing polymerization of the virulence factors. Should the peptide produce an antibody, the antibody would be bound to the peptide and this combination could not attach the subunit of the virulence factor and thereby could not prevent polymerization of the virulence factors.

The applicant respectfully points out also that the comment that the peptide inhibitor may be used in the screening of inhibitors against pathogenic *Escherichia coli* strains is factually not correct, because:

- according to this invention the screening process of potential inhibitors does not use the peptide inhibitor as such, but the idea as shown in Figs. 10A and 10B is that the candidate inhibitor molecule (which may be a peptide or a non-peptide) is added into a mixture of self-polymerizing organelles of a bacterium and by measuring the degree of polymerization of the surface organelle it can be judged if the candidate molecule is an inhibitor or not (if the polymerization of the

subunits of the virulence factor are lowered then the molecule is a good candidate).

Therefore, the argument that the peptides of Group I and II can be used in materially different processes is not true.

It is true as the Examiner states that the sequence in claim 5 is different than that of claim 3; however the applicant wants to point out that the function of the sequences as now reading in the amended claims is the same. The underlining idea of the invention is that the peptide inhibitors prevent polymerization of bacterial virulence organelles and this applies to each claim group.

Based on the above said, the applicant believes that claims of Group I and II overlap in scope and should thus be examined as one invention.

3. The Examiner states that Group I and Group III are distinct because the related inventions do not overlap in scope. The Examiner states that the claims drawn to a bioactive peptide do not overlap the scope of the claims drawn to an antimicrobial peptide as evidenced by the different sequences and functions of the claimed invention. The bioactive peptide has sequence XTXTYY while the antibicrobial peptide has sequence TTGTTKL. Again the Examiner states that the bioactive peptide can be used to produce antibodies while antimicrobial peptide is used in inhibiting the polymerization of haemagglutinin.

In the claims as originally submitted the applicant has used term 'bioactive peptide' in the claims now restricted to Group I, while the applicant used term 'antimicrobial peptide' in claim 8 (the only claim in Group III). The applicant has amended the claims so as to refer to 'antimicrobial peptide' which is according to the terminology in the specification. . The claim 8 has also been amended so as to be dependent of claim 6.

The applicant incorporates herein what is said above about the use of the peptides according to this invention to produce antibodies. There is no such use.

The applicant believes that the inventions of Group I and Group II as now amended are not distinct but overlap in scope as the mode of operation of the peptides is the same, namely the peptides prevent self polymerization of the subunits of the virulence factors.

4. The Examiner states that Group I-II and Group IV are related as product and process of use. The Examiner states however, that the Groups are distinct because the product can be used in materially different process that is distinct from its use in treating a patient with bacterial infection: The bioactive peptide of Group I can be used to produce antibodies against such peptides for use in diagnostics, or the peptide inhibitor of Group II may be used in the screening of inhibitors against pathogenic *E. coli* strains.

As stated already above, the applicant has amended the claims of Group I and II so that each of the claims is toward 'antimicrobial peptide'. The applicant has similarly amended claims 9-14 (Group IV) so that they are all drawn to methods of use of antimicrobial peptide.

Again the applicant respectfully points out that the peptides according to this invention CANNOT be used to produce antibodies due to their shortness. Thus there is no use of Group I claims as production of antibodies for use in diagnostics. Moreover, the suggestion that only Group II peptides could be used in the screening of inhibitors against pathogenic *E. coli* strains is not factually correct as is already stated above that the peptide is not used for the screening, but measurement of the degree of polymerization of bacterium surface organelles is used to judge if a candidate compound can lower the polymerization and therefore has potential as an inhibitor molecule. Therefore, there are no different uses for the peptides now restricted to Group I and II: the antimicrobial peptides (be it Group I or II peptide) can be used for treating patient based on the fact that they are capable of lowering self polymerization of the virulence organelles. Screening of candidate inhibitors is based on the fact that successful inhibitors are

capable to lower self polymerization degree of subunits of bacterial virulence factors and this degree can be measured.

Based on this the applicant believes that Group I-II and IV claims are to be examined together.

5. The Examiner states that Group I-II and Group V are related to product and process of use. The Examiner states that the product and the process of use here are distinct, because the product can be used in a materially different process that is distinct from its use in preventing the polymerization of bacterial protein units. The examiner states that the bioactive peptide of Group I can be used to produce antibodies against such peptides for use in diagnostics, or the peptide inhibitor of Group II may be used in the screening of inhibitors against pathogenic *Escherichia coli* strains. Further, the examiner states that the process of Group V can be practiced with materially different product involving pyranosides that interact with molecular chaperones to disrupt the polymerization of bacterial polymerization units.

The applicant has withdraws Group V claims with traverse. Applicant respectfully incorporates here what is said above about the use of Group I peptides to produce antibodies: there is no such use for these short peptides. Moreover, the applicant incorporates here what is said above about the use of the peptides of Group II in screening of inhibitors against *Escherichia coli* strains: the peptides are not used for this purpose, but the polymerization of the subunits is measured to judge whether or not a candidate molecule is an inhibitor molecule.

The Examiner states the the process of Group V can be practiced with a materially different product, namely with pyranosides. The applicant has amended claim 15 so as to define the structure of the molecule claimed in more details. The applicant believes that the rejection is moot, because the claims of Group V (15 and 16) as now amended are not drawn toward a process but to a product.

6. The Examiner states that Group II and Group III are directed to related products, but are distinct inventions because the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function or effect. The Examiner states the claims drawn to a peptide inhibitor do not overlap the scope of an antimicrobial peptide in both sequence and in function. The peptide inhibitor has sequence TXTYTZ and the antimicrobial has a sequence TTGTTKL. Further, the Examiner states that the peptide inhibitor can be used in materially different process of screening inhibitors against pathogenic *E coli* while the antimicrobial is used in inhibiting the polymerization of haemagglutinin.

The applicant have amended claim 5 (Group II) so as to refer to 'antimicrobial peptide' instead of 'peptide inhibitor' so as to make clear that the mode of function of the peptides of both Group II and III is the same, namely prevention of self polymerization of subunits of the virulence factor.

The Examiner suggests that Group II peptide inhibitors can be used in process for screening inhibitors while Group III is used in inhibiting polymerization of Haemagglutinin. The applicant incorporates herein what is said above about the use of Group II peptides for screening of inhibitors.

The mode of function of the peptide of both Group II and III is the same and the peptides of Group II are not used as such in screening inhibitors. Based on this the applicant believe that Group II and III claims are to be examined together.

7. The Examiner states that even if Group III and IV are related as product and processes of use they are distinct inventions because the product can be used in materially different process that is distinct from its use in treating a patient with bacterial infection. The antimicrobial peptide of Group III can be used to inhibit the polymerization of haemagglutinin. The applicant wish to repeat here, that the underlining function of the peptide inhibitors according to this invention is that they prevent polymerization of

subunits of virulence factors, thereby preventing formation of virulence. Prevention of virulence would prevent bacterial infection in patient. Therefore, preventing polymerization with the antimicrobial peptides is the function whcih then can be applied to treat patients. On the other hand prevention polymerization of haemagglutinin as claimed in claim 8 (Group III) is one embodiment of preventing polymerization of subunits of virulence factor. On page 20 line 22-25 of the specification, the applicant explains how inhibition of Dr adhesin assembly plays a role in the initiation of urinary track infections. Therefore, preventing polymerization of haemagglutinin can be applied to treat or prevent patients to treat microbial infection . Therefore there are no materially different processes distinct from use of the product to treat a patient with bacterial infection.

The applicant believes that the claims of Group III and IV as amended herein are to be examined as one invention.

8. The Examiner states that even if Group III and V are related as product an process of use, the inventions are distinct because the process of Group V can be practiced with a materially different product involving pyranoside that interact with molecular chaperones to disrupt the polymerization of bacterial polymerization units that are materially different from the antimicrobial peptides of Group III.

The applicant has amended claim 15, and believes that it is clear that the claims of Group V are not toward a process but toward a product. Therefore the applicant believes that Group III and V are not distinct inventions.

9. The Examiner states that should either of Group I, II or III be elected, a further election of species is required. Claims 2-4, 5 and 8 are generic. Group I, claim 2 is drawn to the following disclosed patentably distinct species: *Yersinia* and *E. coli*. The species are independent or distinct because they are drawn to different genus's of gram-negative bacterial carrying different genomes encoding for pathogenicity. The Examiner requires

election of a single disclosed species of gram-negative bacteria, even if the requirement is traversed.

The applicant respectfully elects *Eschericia coli* with traverse. Claim 2 is amended accordingly. The traverse is based on the following:

The Applicant has found the phenomenon described in this application by using *Yersinia pestis* adhesin produced in *E.coli*. However, the same binding site of the adhesin of E.coli can be easily recognized, and therefore the applicant believes it is irrelevant that the species are distinct. The applicant strongly believes that both of the species should be allowed in the claim.

10. The Examiner states that in Group I, claim 3 is drawn to the following disclosed patentably distinct species: the amino acid sequence XTXTYY, wherein X is any amino acid and Y is a hydrophobic amino acid. Claim 4 is drawn to the following disclosed patentably distinct species: the amino acid sequence XTXTYY wherein X is any amino acid and Y is either leucine or valine. The Examiner states that the species are independent or distinct because they are drawn to different sequences having different chemical structures. The Examiner requires election of amino acid sequence with completely defined variables X and Y. In essence, all of the variables should be defined by the elected species even though this requirement is traversed.

The applicant elects with traverse the peptide sequence Ala-Thr-Ala-Thr-Leu-Val. Claim 3 is accordingly amended and claim 4 canceled.

The applicant has also amended a new claim 17 depending of claim 2, claiming the element of the antimicrobial peptide consisting of six amino acids. This claim has support in the specification e.g. on page 16 line 4. Claims3 and 5 are now amended so as to be dependent on claim 17.

11. The Examiner states that in Group II, claim 5 is drawn to the following disclosed patentably distinct species: the amino acid sequence TXTYTZ, wherein T is threonine, X is selected from a group consisting of Alanine and Glycine, Y is selected from a group consisting of Alanine, Theronine and Valine and Z is selected from a group consisting of Isoleucine and Valine. Again the Examiner requires election of a single disclosed species of amino acid sequence with completely defined variables X, Y and Z.

The applicant elects with traverse the peptide sequence Thr-Ala-Thr-Val-Thr-Val. Claim 5 is accordingly amended.

12. The Examiner states that claim 8 is drawn to the following disclosed patentably distinct species: the amino acid sequence GTTGTTKL, TTGTTKL and TTKL. The Examiner states that the species are independent and distinct because they are drawn to different sequences having different chemical structures and that the search of the species is not co-extensive.

The applicant elects TTKL with traverse. Claim 8 is amended accordingly. The applicant points out that the longer sequence GTTGTTKL and TTGTTKL both comprise the now elected sequence TTKL and therefore the examination should not be an undue burden.

CONCLUSION

A restriction to one of five (5) distinct inventions is required under 35 U.S.C. Section 121. Hereby, the applicant provisionally and respectfully elects Group I with traverse.

The Applicant believes that the claims as amended and further the arguments as stated above makes the restriction requirement between inventions not applicable anymore. The Applicant respectfully requests consideration of the amended claims without restriction.

DODDS AND ASSOCIATES

By:
/Maie Mo/
Leea Susanne Somersalo
L0092

cc. file
Timo Korpela
Tarja Enala